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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,981	01/26/2006	Shigeyoshi Nishino	740709-551	9439
22204 7590 12/15/2008 NIXON PEABODY, LLP 401 9TH STREET, NW SUITE 900 WASHINGTON, DC 20004-2128			EXAMINER WILLIS, DOUGLAS M	
			ART UNIT 1624	PAPER NUMBER
			MAIL DATE 12/15/2008	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/565,981

Applicant(s)

NISHINO ET AL.

Examiner

DOUGLAS M. WILLIS

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 October 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 7 and 8 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 7 and 8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/ISD/IC)
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____
- Paper No(s)/Mail Date 01-26-06; 07-24-06; 09-26-06

DETAILED ACTION

Status of the Claims / Priority

Claims 1-4, 7 and 8 are pending in the current application. According to the *In The Claims*, filed October 28, 2008, claims 1-4 were amended and claims 5 and 6 were cancelled. This application is a 35 U.S.C. § 371 National Stage Filing of International Application No. PCT/JP2004/010965, filed July 30, 2004, which claims priority under 35 U.S.C. § 119(a-d) to JP 2003-282696, filed July 30, 2003.

Thus, a second Office action on the merits of claims 1-4, 7 and 8 is contained within.

Status of Claim Objections

Applicant's arguments, on page 4 of the *Remarks*, filed October 28, 2008, with respect to claim 6, have been fully considered and are persuasive. Consequently, the objection of claim 6, made in the *Non-Final Rejection*, mailed on May 28, 2008, has been withdrawn in light of the *In The Claims*, (amendments) filed October 28, 2008, whereby claim 6 was cancelled by applicant.

Status of Claim Rejections - 35 U.S.C. § 102

Applicant's arguments, on pages 4 and 5 of the *Remarks*, filed October 28, 2008, with respect to claims 5 and 6, have been fully considered and are persuasive. Consequently, the rejection of claims 5 and 6, made in the *Non-Final Rejection*, mailed on May 28, 2008, has been withdrawn in light of the *In The Claims* (amendments), filed October 28, 2008, whereby claims 5 and 6 were cancelled by applicant.

Applicant's arguments, on pages 5 and 6 of the *Remarks*, filed October 28, 2008, with respect to claim 1, have been fully considered and are persuasive. Consequently, the rejection of

claim 1, made in the *Non-Final Rejection*, mailed on May 28, 2008, has been withdrawn in light of the *In The Claims* (amendments), filed October 28, 2008, whereby the foreign priority was perfected to antedate the reference and overcome the rejection.

Status of Claim Rejections - 35 U.S.C. § 103

Applicant's arguments, on pages 5 and 6 of the *Remarks*, filed October 28, 2008, with respect to claims 2-4, 7 and 8, have been fully considered, but are moot in view of the new ground(s) of rejection.

New Specification Objection

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

- (a) TITLE OF THE INVENTION.
- (b) CROSS-REFERENCE TO RELATED APPLICATIONS.
- (c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
- (d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
- (e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
- (f) BACKGROUND OF THE INVENTION.
 - (1) Field of the Invention.
 - (2) Description of Related Art (including information disclosed under 37 CFR 1.97 and 1.98).

- (g) BRIEF SUMMARY OF THE INVENTION.
- (h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
- (i) DETAILED DESCRIPTION OF THE INVENTION.
- (j) CLAIM OR CLAIMS (commencing on a separate sheet).
- (k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
- (l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825).

Applicant is advised to format the specification according to 37 CFR 1.77(b) above. Revisions should particularly include and/or address sections (b-c) and (h). Appropriate correction is required.

New Specification Objection - Abstract

Applicant is reminded of the proper content of an abstract of the disclosure.

With regard particularly to chemical patents, for compounds or compositions, the general nature of the compound or composition should be given as well as the use thereof, e.g., *The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral anti-diabetics.* Exemplification of a species could be illustrative of members of the class. For processes, the reactions, reagents and process conditions should be stated, generally illustrated by a single example, unless variations are necessary. See MPEP § 608.01(b), Section B.

The abstract of the disclosure is objected to because it neither provides a general reaction scheme nor exemplifies any members or formulae illustrative of the recited compound(s). Correction is required. See MPEP § 608.01(b).

New Claim Rejections - 35 U.S.C. § 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

- (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art

are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Amended claims 1-4, and dependent claims 7 and 8 are newly rejected under 35 U.S.C. § 103(a) as being unpatentable over Katsuyuki, et al. in JP 2002-293773 (previously cited), in view of Wang, et al. in WO 03/000188 and Scarborough, et al. in US 3,119,824 (newly cited in view of the amendments).

The instant application recites a process for preparation of 6,7-bis(2-methoxyethoxy)quinazolin-4-one, which comprises the steps in order of: causing a reaction of ethyl 3,4-dihydroxybenzoate with 2-chloroethyl methyl ether, in an organic solvent and the presence of a base, to afford ethyl 3,4-bis(2-methoxyethoxy)benzoate; causing a reaction of ethyl 3,4-bis(2-methoxyethoxy)benzoate with nitric acid, in the presence of sulfuric acid, to afford ethyl 4,5-bis(2-methoxyethoxy)-2-nitrobenzoate; causing a reaction of ethyl 4,5-bis(2-methoxyethoxy)-2-nitrobenzoate with hydrogen, in the presence of a metallic catalyst, to afford ethyl 2-amino-4,5-bis(2-methoxyethoxy)benzoate; and causing a reaction of the ethyl 2-amino-4,5-bis(2-methoxyethoxy)benzoate with an orthoformic ester, in the presence of ammonium acetate, to afford 6,7-bis(2-methoxyethoxy)quinazolin-4-one.

Katsuyuki, et al. (JP 2002-293773), in the English translation provided in the file and as cited on the IDS, teaches a process for the preparation of a tautomer of 6,7-bis(2-

methoxyethoxy)quinazoline-4-one, which comprises the steps in order of [p. 5, ¶ 19]: causing a reaction of ethyl 3,4-dihydroxybenzoate with 2-methoxyethyl methanesulfonate, in acetone and in the presence of potassium carbonate, to afford ethyl 3,4-bis(2-methoxyethoxy)benzoate [p. 5, ¶ 7-10]; causing a reaction of ethyl 3,4-bis(2-methoxyethoxy)benzoate with nitric acid, in the presence of sulfuric acid, to afford ethyl 4,5-bis(2-methoxyethoxy)-2-nitrobenzoate [p. 5, ¶ 11-12]; causing a reaction of ethyl 4,5-bis(2-methoxyethoxy)-2-nitrobenzoate with hydrogen, in the presence of a platinum catalyst, to afford ethyl 2-amino-4,5-bis(2-methoxyethoxy)benzoate [p. 6, ¶ 13-15]; and causing a reaction of ethyl 2-amino-4,5-bis(2-methoxyethoxy)benzoate, with ammonium formate, to afford 6,7-bis(2-methoxyethoxy)quinazoline-4-one [p. 6, ¶ 16-19]. Furthermore, Katsuyuki, in the genus disclosure, teaches ammonium formate as a versatile reagent that serves as both a formic acid compound and ammonium carboxylate (source of necessary amine or ammonia base) [p. 6, ¶ 16-19].

Wang, et al. (WO 03/000188) teaches a process for the preparation of 6,7-bis(2-methoxyethoxy)quinazoline-4-one, which comprises at least the step of causing a reaction of ethyl 3,4-dihydroxybenzoate with 2-bromoethyl methyl ether, in acetone and in the presence of potassium carbonate, to afford ethyl 3,4-bis(2-methoxyethoxy)benzoate [p. 106, Scheme 12].

Scarborough, et al. (US 3,119,824) teaches a process for the preparation of substituted quinazoline-4-ones, wherein ethyl orthoformate is used as the formic acid source for ring closure [Method C, column 4, line 69].

The only difference between the applicant's instantly recited process for preparation of 6,7-bis(2-methoxy-ethoxy)quinazolin-4-one and Katsuyuki's process for preparation of 6,7-bis(2-methoxy-ethoxy)quinazolin-4-one is optimization of experimental conditions. For

instance, a) chloroethyl methyl ether is used as the alkylating agent in step 1 of the instantly recited process for preparation of 6,7-bis(2-methoxyethoxy)quinazolin-4-one, whereas 2-methoxyethyl methanesulfonate is used as the alkylating agent in step 1 of Katsuyaki's process for preparation of 6,7-bis(2-methoxyethoxy)quinazolin-4-one; and b) methyl orthoformate is used as the formic acid source for ring closure in step 4 of the instantly recited process for preparation of 6,7-bis(2-methoxyethoxy)quinazolin-4-one, whereas ammonium formate is used as the formic acid source for ring closure in step 4 of Katsuyaki's process for preparation of 6,7-bis(2-methoxyethoxy)-quinazolin-4-one.

The courts have recognized that *the adjustment of experimental parameters, reaction conditions or purification/isolation technique, as well as adjustment of reaction temperature, reaction time, solvent employed and reagent choice, is merely deemed a matter of judicious selection and routine optimization, which is well within the purview of the skilled artisan.* (see *In re Mostovych*, Weber, Mitchell and Aulbach, 144 USPQ 38).

Moreover, the MPEP § 2144.05, Section II states and the courts further recognize that *generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art, unless there is evidence indicating such concentration or temperature is critical and that where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.* {see *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); see also *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382; for more recent cases applying this principle, see *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), *cert. denied*, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056

(Fed. Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997)}.

Similarly, the courts have recognized that *variations of particular work available in one field of endeavor may be prompted by design incentives and other market forces, either in the same field or a different one, and if a person of ordinary skill in the art can implement a predictable variation, 35 U.S.C. § 103 likely bars its patentability.* (see *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385).

Furthermore, the *fact that a claimed combination of elements was “obvious to try” may be used to show that such a combination was obvious under 35 U.S.C. § 103, since, if there is design need or market pressure to solve a problem, and there are a finite number of identified, predictable solutions, a person of ordinary skill in the art has good reason to pursue known options within his or her technical grasp, and if this leads to anticipated success, it is likely the product of ordinary skill and common sense, not innovation.* (see *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385).

Consequently, since: a) Katsuyaki teaches a process for preparation of 6,7-bis(2-methoxyethoxy)quinazolin-4-one, comprising four steps identical to those of the instantly recited process for preparation of 6,7-bis(2-methoxyethoxy)quinazolin-4-one, wherein 2-methoxyethyl methanesulfonate is used as the alkylating agent in step 1 and ammonium formate is used as the formic acid source for ring closure in step 4; b) Katsuyuki teaches a process for preparation of 6,7-bis(2-methoxyethoxy)quinazolin-4-one, where, in step 4, ammonium formate serves as a formic acid compound and carboxylate source of ammonia base; c) Wang teaches a process for preparation of 6,7-bis(2-methoxyethoxy)quinazolin-4-one, comprising four steps identical to those of the instantly recited process for preparation of 6,7-bis(2-methoxyethoxy)quinazolin-4-

one, wherein bromoethyl methyl ether is alternatively used as an alkylating agent; d) Scarborough teaches a process for the preparation of substituted quinazoline-4-ones, wherein ethyl orthoformate is alternatively used as the formic acid source for ring closure; e) the courts have recognized that *the adjustment of experimental parameters, reaction conditions or purification/isolation technique is merely deemed a matter of judicious selection and routine optimization, which is well within the purview of the skilled artisan*, and f) the courts have further recognized that *if a person of ordinary skill in the art can implement a predictable variation of particular work available in one field of endeavor 35 U.S.C. § 103 likely bars its patentability*, one having ordinary skill in the art, at the time this invention was made, would have been motivated to combine the teachings of Katsuyuki, Wang and Scarborough and try appropriate alternative reagents, such as haloethyl methyl ethers as alkylating agents (i.e. chloroethyl methyl ether) and alkyl orthoformate esters (i.e. methyl orthoformate), during optimization of experimental conditions in Katsuyuki's four-step process for the preparation of 6,7-bis(2-methoxyethoxy)-quinazolin-4-one, with a reasonable expectation of success, rendering claims 1-4, 7 and 8 obvious.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DOUGLAS M. WILLIS, whose telephone number is 571-270-5757. The examiner can normally be reached on Monday thru Thursday from 8:00-6:00 EST. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson, can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/DOUGLAS M WILLIS/
Examiner, Art Unit 1624

/James O. Wilson/
Supervisory Patent Examiner, Art Unit 1624